In The Specification

Please delete the paragraph starting on page 6, line 16 and insert the following paragraph:

B1

--This invention provides an isolated nucleic acid molecule comprising at least 15 contiguous nucleotides capable of specifically hybridizing with a unique sequence included within the sequence of the isolated nucleic acid molecule encoding IRTA protein. In an embodiment, the IRTA protein may be IRTA1, IRTA2, IRTA3, IRTA4 or IRTA5 protein, or fragment(s) thereof, having the amino acid sequence set forth in any of Figures 18A (SEQ ID NO:1), 18B-1-18B-3 (SEQ ID NOs:3, 41, 44), 18C-1-18C-2 (SEQ ID NO:5), 18D-1-18D-2 (SEQ ID NO:7) or 18E-1-18E-2 (SEQ ID NO:9), respectively.--

Please delete the paragraph starting on page 7, line 23 and insert the following paragraph:

B2

--This invention provides a purified IRTA2 protein comprising an amino acid sequence set forth in Figures 18B-1-18B-3 (SEQ ID NO:41, SEQ ID NO:3, SEQ ID NO:44).--

Please delete the paragraph starting on page 11, line 2 and insert the following paragraph:

B3

--**Figures 1A-1B.** Molecular cloning of the translocation t(1;14)(q21;q32) in the FR4 multiple myeloma cell line. Fig. 1A) Schematic representation of the λFR4B-5 and λFR4S-a

clones, representing der(14) and der(1) breakpoints, and of the germline IgH and 1q21 loci. Fig. 1B) Nucleotide sequence of the breakpoint junction (SEQ ID NO:12) and its alignment to the corresponding germline regions of chromosome 14 (SEQ ID NO:13). Chr 1 is SEQ ID NO:11. Sα, IgA switch region; LCR: 3' IgH locus control region; B, *BamHI*; H, *HindIII*; X, *XhoI*.

Please delete the paragraph starting on page 16, line 24 and insert the following paragraph:

Figure 5. Nucleotide and amino acid sequence of human MUM2 (SEQ ID NO:14 and SEQ ID NO:15, respectively). The deduced amino acid sequence is shown above the nucleotide sequence in one-letter code and is numbered on the right, with position 1 set to the first codon of the signal peptide. The predicted signal peptidase site was derived by a computer algorithm described in Nielsen et al., Protein Engineering 10, 1-6 (1997) and is marked by an arrowhead. The polyadenylation signal AATAAA is underlined. Potential sites for N-glycosylation are also underlined in the amino acid sequence. A hydrophobic stretch of 16 amino acids predicted to span the plasma membrane is doubly underlined. Consensus SH2-binding

B4

sites are highlighted by a wavy underline.--

Please delete the paragraph starting on page 17, line 11 and insert the following paragraph:

--**Figure 6A.** Nucleotide and amino acid sequence of human MUM3-a (SEQ ID NO:16 and SEQ ID NO:17, respectively). The deduced amino acid sequence is shown above the nucleotide sequence in one-letter code and is numbered on the right, with position 1 set to the first codon of the signal peptide. The predicted site for signal peptidase cleavage was derived as previously stated above and is marked by an arrowhead. The polyadenylation signal ATTAAA is underlined. Potential sites for N-glycosylation are also underlined in the amino acid sequence. The protein lacks a transmembrane domain and is predicted to be secreted.--

B5

Please delete the paragraph starting on page 17, line 26 and insert the following paragraph:

--**Figure 6B.** Nucleotide and amino acid sequence of human MUM3-b (SEQ ID NO:18 and SEQ ID NO:19, respectively). The deduced amino acid sequence is shown above the nucleotide sequence in one-letter code and is numbered on the right, with position 1 set to the first codon of the signal peptide. The predicted site for signal peptidase cleavage was derived as previously stated above and is marked by an

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arrowhead. The polyadenylation signal AATAAA is underlined. Potential sites for N-glycosylation are underlined in the amino acid sequence.--

Please delete the paragraph starting on page 18, line 7 and insert the following paragraph:

--**Figure 6C-1-6C-2**. Nucleotide and amino acid sequence of human MUM3-c (SEQ ID NO:20 and SEQ ID NO:21, respectively). The deduced amino acid sequence is shown above the nucleotide sequence in one-letter code and is numbered on the right, with position 1 set to the first codon of the signal peptide. The predicted site for signal peptidase cleavage was derived as previously stated above and is marked by an arrowhead. The polyadenylation signal AATAAA is underlined. Potential sites for N-glycosylation are underlined in the amino acid sequence. A hydrophobic stretch of 23 amino acids predicted to span the plasma membrane is doubly underlined. Consensus SH2-binding sites are highlighted by a wavy underline.--

B7

Please delete the paragraph starting on page 18, line 27 and insert the following paragraph:

--**Figures 7A-7C**. t(1;14)(q21;32) in FR4 generates a MUM2/Ca fusion transcript. (Fig. 7A) Schematic

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representation of ther der(14) genomic clone λFR4B-5 and of the germline IgHA1 locus. The FR4 breakpoint is marked by an arrow. Filled and open boxes represent the MUM2 and Calpha coding and non-coding exons respectively. The position of the MUM2 exon 1 probe used for Northern blot analysis is shown by a bar. (Fig. 7B) Northern blot analysis with a MUM2 exon 1 probe on FR4 and additional cell lines detects an abnormal message of 0.8 Kb, selectively in FR4. Arrowheads point to the location of normal MUM2 message in EREB mRNA. JJN3 and U266, myeloma cell lines; EREB, conditional EBV-transformed B lymphoblastoid cell line. Two μg of polyA+ RNA were loaded per lane. (Fig. 7C) Nucleotide and amino acid sequence of the MUM2-Ca fusion cDNA in FR4 (SEQ ID NO:23 and SEQ ID NO:22, respectively). The cDNA was amplified by RT-PCR from FR4 total RNA using the primers shown in Fig. 7A, and was subsequently subcloned and sequenced. The deduced amino acid sequence is shown above the nucleotide sequence in one-letter code and is numbered on the right with position 1 set to the first codon of the signal peptide. The predicted site for signal peptidase cleavage was derived as previously stated above and is marked by an arrowhead. The polyadenylation signal AATAAA is underlined. The Calpha

transmembrane domain is underlined. The MUM2 portion of the cDNA is shown on italics. H, HindIII; B, BamHI; X, XhoI; Sα, IgA switch region; EC, extracellular region; TM, transmembrane; CYT, cytoplasmic domain.

Please delete the paragraph starting on page 20, line 4 and insert the following paragraph:

Figures 8A-8C. Molecular cloning of the translocation t(1;14)(q21;q32) in the FR4 multiple myeloma cell line. (Fig. 8A) Schematic representation of the phage clones representing der(14) and der(1) breakpoints and the germline IGH and 1q21 loci. Chromosome 14 sequences are indicated by a solid black line with black boxes representing Ca1 exons. Chromosome 1 sequences are shown as a grey line. The probes used for chromosomal mapping are indicated below the map. Restriction enzyme codes are: B, BamHI; H, HindIII; X, XhoI; S, SacI; E, EcoRI. For enzymes marked by (*) only sites delineating the probes are shown. Sa: IgA switch region; LCR: 3'IgH locus control region. (Fig. 8B) Nucleotide sequence of the breakpoint junctions (SEQ ID NO:25 and SEQ ID NO:27). and their alignment to the corresponding germline regions of chromosomes 14 and 1 (SEQ ID NO:24 and SEQ

ID NO:26, respectively). (Fig. 8C) Left, fluorescence in situ hybridization (FISH) analysis on human normal metaphase spreads with the PAC clone 49A16 (Fig. 13) spanning the germline1q21 region at the FR4 breakpoint. Right, DAPI stained image from the same metaphase spread.--

Please delete the paragraph starting on page 21, line 27 and insert the following paragraph:

--**Figures 10A-10B.** Comparison of the amino acid sequences of IRTA1 (SEQ ID NO:32) and IRTA2 (SEQ ID NO:33) with members of the Fc Receptor family (Fig. 10A) Multiple sequence alignment of the first two (top) and the third (bottom) extracellular Ig-domains of IRTA1 and IRTA2 to Fc receptor family members; FCGRIIA (SEQ ID NO:28), FCGRIIIA (SEQ ID NO:29), FCERIA (SEQ ID NO:30), and FCGRIA (SEQ ID NO:31). The sequences were compared using the ClustalW program (Thompson et al., 1994). Black-shaded boxes indicate conserved aminoacids among all sequences; dark-grey shaded boxes indicate conserved aminoacids among at least half of the sequences; light-shaded boxes indicate conservative substitutions. (Fig. 10B) Alignment of the SH2-binding domains of IRTA1 (SEQ ID NO:35) and IRTA2 (SEQ ID NO:37) with the ITAM (SEQ ID NO:34) and ITIM

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(SEQ ID NO:39) consensus motifs. Conserved amino acid positions are in bold. BGP is SEQ ID NO:38 and PECAM is SEQ ID NO:36. Symbol X represents any amino acid.--

Please delete the paragraph starting on page 27, line 30 and insert the following paragraph:

B11

--**Figure 18A**. IRTA1 cDNA (SEQ ID NO:2) and the amino acid sequence (SEQ ID NO:1) of the encoded IRTA1 protein.--

Please delete the paragraph starting on page 28, line 1 and insert the following paragraph:

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--**Figures 18B-1-18B-3**. IRTA2 cDNA (2a, SEQ ID NO:43; 2b, SEQ ID NO:4; 2c, SEQ ID NO:40) and the amino acid sequence (2a, SEQ ID NO:44; 2b, SEQ ID NO:3; 2c, SEQ ID NO:41) of the encoded IRTA2 protein.--

Please delete the paragraph starting on page 28, line 5 and insert the following paragraph:

B13

--**Figures 18C-1-18C-2**. IRTA3 cDNA (SEQ ID NO:6) and the amino acid sequence (SEQ ID NO:5) of the encoded IRTA3 protein.--

Please delete the paragraph starting on page 28, line 9 and insert the following paragraph:

B14 --**Figures 18D-1-18D-2**. IRTA4 cDNA (SEQ ID NO:8) and the amino acid sequence (SEQ ID NO:7) of the encoded IRTA4 protein.--

Please delete the paragraph starting on page 28, line 13 and insert the following paragraph:

B15 --**Figures 18E-1-18E-2**. IRTA5 cDNA (SEQ ID NO:10) and the amino acid sequence (SEQ ID NO:9) of the encoded IRTA5 protein.--

Please delete the paragraph starting on page 30, line 4 and insert the following paragraph:

B16 --In another embodiment of the above-described isolated nucleic acid molecule, the encoded IRTA protein is IRTA2 protein comprising the amino acid sequence set forth in Figures 18B-1-18B-3 (SEQ ID NO:44; SEQ ID NO:3; SEQ ID NO:41).--

Please delete the paragraph starting on page 30, line 24 and insert the following paragraph:

B17 --In another embodiment of any of the above-described isolated nucleic acid molecules, the nucleic acid molecule is DNA. In further embodiments, the DNA is cDNA. In additional embodiments, the DNA is genomic DNA. In another embodiment, the nucleic acid molecule is an RNA molecule. In yet another embodiment, the DNA molecule is cDNA having the nucleotide sequence set forth in Figure 18A (SEQ ID NO:2). In another embodiment, the DNA

molecule is cDNA having the nucleotide sequence set forth in Figure 18B (SEQ ID NO:43; SEQ ID NO:4; SEQ ID NO:40). In a further embodiment, the DNA molecule is cDNA having the nucleotide sequence set forth in Figure 18C (SEQ ID NO:6). In another embodiment, the DNA molecule is cDNA having the nucleotide sequence set forth in Figure 18D (SEQ ID NO:8). In an embodiment, the DNA molecule is cDNA having the nucleotide sequence set forth in Figure 18E (SEQ ID NO:10). In preferred embodiments of the isolated nucleic acid molecule, wherein the nucleic acid molecules encode human IRTA1, IRTA2, IRTA3, IRTA4 or IRTA5 protein. In additional embodiments, the nucleic acid molecules encode mammalian IRTA1 protein. The mammalian IRTA1 protein may be murine IRTA1 protein. In another preferred embodiment, the isolated nucleic acid molecules are operatively linked to a promoter of DNA transcription. In yet another preferred embodiment of the isolated nucleic acid molecule, the promoter comprises a bacterial, yeast, insect, plant or mammalian promoter.

B17 cl

Please delete the paragraph starting on page 39, line 31 and insert the following paragraph:

--This invention provides a purified IRTA2 protein comprising the amino acid sequence set forth in Figures 18B-1-18B-3 (SEQ ID NO:44; SEQ ID NO:3; SEQ ID NO:41). In an embodiment of the purified IRTA2 protein, the IRTA2 protein is human IRTA2.--

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Please delete the paragraph starting on page 63, line 28 and insert the following paragraph:

--Sequence analysis of the breakpoint regions on the derivative

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Ins C19

chromosomes and alignment with the germline 14q32 and 1q21 loci revealed that the breakpoint had occurred in the intron between the CH3 and the transmembrane exon of $C\alpha_1$ on chromosome 14. Although the breakpoint region was devoid of recombination signal sequences (RSS) or switch signal sequences (Kuppers et al., 1999), the sequence CTTAAC (underlined on Figure 8B) was present in both germline chromosomes 14 and 1 at the breakpoint junction. One copy of this sequence was present in each of the derivative chromosomes, with a slight modification in the der(1) copy (point mutation in the last nucleotide: C to G). The nucleotides AT preceding CTTAAC on chromosome 1 were also present in both derivative chromosomes (Figure 8B). The translocation did not result in any loss of chromosome 1 sequences. On the other hand, in the chromosome 14 portion of der(1) we observed two deletions upstream of the breakpoint junction: a 16 nucleotide deletion (GGCACCTCCCCTTAAC) (SEQ ID NO:42) and a 4 nucleotide deletion (TGCA) 6 nucleotides upstream (Figure 8B). These observations indicate that the t(1;14)(q21;q32) in FR4 cells represents a balanced reciprocal translocation possibly facilitated by the presence of homologous sequences (CTTAAC) on both chromosomes.

In The Claims

Please amend claims 3, 12-15 and 35 as follows:

3. (Amended) The isolated nucleic acid molecule of claim 1, wherein the IRTA protein is an IRTA2 protein comprising an amino acid sequence set forth in SEQ ID NO:3, SEQ ID NO:41 or SEQ ID NO:44.

12. (Amended) The isolated DNA molecule of claim 2, wherein the DNA molecule is cDNA having a nucleotide sequence set forth in SEQ ID NO:4, SEQ ID NO:40 or SEQ ID NO:43.

13. (Amended) The isolated DNA molecule of claim 2, wherein the DNA molecule is cDNA having the nucleotide sequence set forth in Figure 18C (SEQ ID NO:6).

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14. (Amended) The isolated DNA molecule of claim 2, wherein the DNA molecule is cDNA having the nucleotide sequence set forth in Figure 18D (SEQ ID NO:8).

15. (Amended) The isolated DNA molecule of claim 2, wherein the DNA molecule is cDNA having the nucleotide sequence set forth in Figure 18E (SEQ ID NO:10).

35. (Amended) A purified IRTA2 protein comprising an amino acid sequence set forth in SEQ ID NO:3, SEQ ID NO:41 or SEQ ID NO:44.

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REMARKS

Claims 1-25 and 33-47 are pending and under examination. Applicant has hereinabove amended claims 3, 12-15 and 35. Accordingly, after entry of this Amendment, claims 1-25 and 33-47 will be pending.

In the March 26, 2002 Communication, the Examiner stated that the Sequence Listing filed January 14, 2002 does not correlate with the sequences as set forth in the specification. Accordingly, the Examiner required appropriate correction via amendment and/or submission of a corrected Sequence Listing.